

## Original Article

# Accuracy of cardiac output measurements with pulse contour analysis (PulseCO<sup>TM</sup>) and Doppler echocardiography during off-pump coronary artery bypass grafting

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## Summary

**Background and objective:** During off-pump coronary bypass grafting, surgical manipulation and dislocation of the heart may cause cardiovascular instability. Monitoring of cardiac output facilitates intraoperative haemodynamic management but pulmonary artery catheters are often considered too invasive. Pulse contour analysis and transoesophageal echocardiography could serve as alternatives, but there is controversy about their accuracies. We validated pulse contour analysis using a standard radial arterial catheter (PulseCO<sup>TM</sup>) and aortic Doppler flowmetry with transoesophageal echocardiography in patients undergoing off-pump coronary bypass surgery. Pulmonary arterial thermodilution served as the reference technique. **Methods:** In 20 patients undergoing off-pump coronary bypass, cardiac output was measured with bolus thermodilution (CO<sub>TD</sub>), pulse contour analysis (CO<sub>PC</sub>), and transoesophageal echocardiography (CO<sub>echo</sub>) at fixed time intervals during the procedure. Data were compared using linear regression and Bland–Altman analysis. At the end of the procedure, dobutamine was infused at a rate of 2.5 µg kg<sup>-1</sup> min<sup>-1</sup> in six patients to study the agreement between methods in quantifying changes in cardiac output. **Results:** Comparison between CO<sub>PC</sub> and CO<sub>TD</sub> showed a bias ± limits of agreement of  $-0.03 \pm 1.30$  L min<sup>-1</sup> (mean error 29%). Doppler echocardiography was not always feasible when the heart was displaced from the oesophagus and had lower accuracy: bias ± limits of agreement vs. CO<sub>TD</sub> was  $0.45 \pm 1.93$  (mean error 43%). Increases in cardiac output induced by dobutamine were well quantified both by pulse contour analysis (CO<sub>PC</sub> =  $0.76 \times \text{CO}_{TD} + 0.58$ ;  $r^2 = 0.65$ ) and Doppler, although the latter tended to overestimate these changes (CO<sub>echo</sub> =  $1.58 \times \text{CO}_{TD} - 0.13$ ;  $r^2 = 0.53$ ). **Conclusions:** Calibrated pulse contour analysis using the PulseCO system is an acceptable technique to measure cardiac output non-invasively in off-pump coronary bypass patients. Doppler echocardiography performs less well and is not always feasible with transoesophageal echocardiography when the heart is displaced.

**Keywords:** SURGERY CARDIAC; CORONARY ARTERY BYPASS GRAFTING; CORONARY ARTERY BYPASS OFF-PUMP; CARDIAC OUTPUT; PHYSIOLOGIC MONITORING.

## Introduction

During off-pump coronary artery bypass (OPCAB) surgery, direct manipulation and dislocation of the

heart, as well as the repetitive induction of working heart ischaemia during distal coronary anastomosis, may significantly disrupt circulatory homeostasis [1] and challenge the anaesthesiologist to preserve circulatory homeostasis during this procedure. Reliable monitoring tools are a prerequisite for adequate haemodynamic management; however, consensus about which techniques to use for this purpose is lacking. While pulmonary arterial (PA) thermodilution has

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long been the only reliable clinical method to quantify cardiac output (CO), there is growing concern about the risks associated with this invasive procedure. Moreover, up to now haemodynamic monitoring based on the PA catheter has not been shown to result in better clinical outcomes [2–6].

More recently, pulse contour analysis (PCA) has been adopted in clinical practice as a less invasive alternative to PA catheters [7,8]. The technology is appealing since it derives CO from an arterial waveform and provides continuous data with a very fast response time. Several PCA devices are now commercially available which all differ with regard to the underlying algorithm, calibration method and the eventual need for specific equipment. The PulseCO<sup>TM</sup> system (LiDCO Ltd, Cambridge, UK) is of particular clinical interest since it derives CO from a standard radial arterial catheter and does not require a special transducer. Because this particular system has not been extensively validated in clinical studies, our primary goal was to prospectively assess its accuracy in a dynamic environment such as OPCAB surgery. We also evaluated the clinical accuracy of Doppler-based CO measurements. Echocardiography is an invaluable technique both for monitoring and diagnosis in cardiac anaesthesia but its accuracy in quantifying CO has recently been questioned [9,10]. Both techniques were compared with PA thermodilution as the clinical reference, routinely used to monitor patients undergoing OPCAB surgery in our institution.

## Methods

The study was approved by the institutional Ethics Committee and written informed consent was obtained from each patient on the day before surgery. Twenty patients scheduled to undergo elective OPCAB surgery participated in this study. Significant aortic valve lesions (aortic regurgitation  $>1/4$  and peak aortic gradient  $>25$  mmHg) and/or documented arrhythmias were considered exclusion criteria. Patients were premedicated with sublingual lorazepam ( $0.05$  mg kg<sup>-1</sup>). A 20-G arterial catheter was inserted in the left radial artery and connected to the PulseCO Haemodynamic Monitor (LiDCO Ltd, London, England). Anaesthesia was induced with midazolam ( $0.05$  mg kg<sup>-1</sup>), propofol (target control infusion at  $1$  µg mL<sup>-1</sup>), pancuronium ( $0.1$  mg kg<sup>-1</sup>) and sufentanil ( $0.75$  µg kg<sup>-1</sup>). A 7.5-Fr thermodilution PA-catheter (Paceport, Edwards Lifesciences, Saint-Prex, Switzerland) was introduced via the right internal jugular vein and connected to the CO module of a Solar 9500 patient monitoring system (GE Medical Waukesha, Wisconsin, USA). A transoesophageal echoprobe with a 7 MHz transducer was

placed and connected to a GE Vivid 5 ultrasound system (GE VingMed, Horten, Norway).

CO was measured using three different techniques in random order: bolus thermodilution (CO<sub>TD</sub>) was performed in triplicate with injections of 10 mL iced saline and the results were averaged. PCA (CO<sub>PC</sub>) was obtained from the radial arterial pressure signal processed by the PulseCO system (LiDCO Ltd, Cambridge, UK). The average of a 1-min continuous registration was taken as the representative result. The PulseCO monitor was calibrated at the start of the procedure using the first set of measurements with CO<sub>TD</sub>. No additional calibrations were performed during the remaining study period. CO<sub>PC</sub> data obtained during initial calibration were excluded from analysis. EchoDoppler measurements (CO<sub>echo</sub>) consisted of transaortic flow velocity determinations using continuous wave Doppler from the deep transgastric position [11]. Stroke volume was calculated as the product of the manually traced velocity time integral (VTI) of aortic outflow and the aortic valvular orifice area. Aortic valve orifice area was calculated using the triangular shape assumption of valve opening [10,12]. For each measurement period, the aortic VTI's of three consecutive beats were averaged.

A complete data set was collected after induction of anaesthesia and again every 30 min until the end of the surgical procedure. Measurements started only when steady-state conditions were achieved and the data were discarded if haemodynamic variables varied more than 15% during the acquisition period. In a subset of six patients, additional measurements of CO<sub>echo</sub>, CO<sub>TD</sub> and CO<sub>PC</sub> were performed before and after a 15-min dobutamine infusion at a rate of  $2.5$  µg kg<sup>-1</sup> min<sup>-1</sup>. For this part of the study protocol, we selected only patients who would benefit from inotropic support after revascularization and excluded those with a baseline cardiac index higher than  $3$  L min<sup>-1</sup> m<sup>-2</sup>, documented left ventricular hypertrophy, incomplete revascularization or haemoglobin levels lower than  $9$  g dL<sup>-1</sup>.

The three different methods were compared with Bland–Altman and linear regression analysis [13]. Limits of agreement were considered clinically acceptable if lower than 30% of the mean value [14]. Haemodynamic variables before and after dobutamine infusion were analysed using the paired *t*-test. Changes in CO after dobutamine infusion were compared using linear regression analysis. A value of  $\alpha < 0.05$  was considered statistically significant.

## Results

The study population consisted of 15 male and 5 female patients (age  $68 \pm 12$  yr, height  $168 \pm 9$  cm,



body weight  $78 \pm 12$  kg; mean  $\pm$  SD). In each patient, at least five coupled measurements of  $\text{CO}_{\text{TD}}$  and  $\text{CO}_{\text{PC}}$  were made. In two patients, we failed to consistently align the Doppler beam to the direction of aortic flow with the transducer in the deep trans-gastric position. This problem occurred in most subjects at the time the heart was tilted and displaced. Consequently, the total number of  $\text{CO}_{\text{echo}}$  measurements included for analysis was lower (84 vs. 149  $\text{CO}_{\text{PC}}$ ).  $\text{CO}_{\text{PC}}$  closely correlated ( $r^2 = 0.70$ ,  $P < 0.0001$ ) with  $\text{CO}_{\text{TD}}$  and displayed a bias of  $-0.03 \text{ L min}^{-1}$ , with limits of agreement from 1.26 to  $-1.33 \text{ L min}^{-1}$  (29% of the mean value) (Fig. 1).  $\text{CO}_{\text{echo}}$  also correlated ( $r^2 = 0.46$ ,  $P < 0.0001$ ) well with  $\text{CO}_{\text{TD}}$  but displayed a much larger bias ( $0.45 \text{ L min}^{-1}$ ) and wider limits of agreement (2.38 and  $-1.49 \text{ L min}^{-1}$ , i.e. 43% of the mean value) (Fig. 2). Calibration of the  $\text{CO}_{\text{echo}}$  data against using the first  $\text{CO}_{\text{TD}}$  measurement – analogous to the  $\text{CO}_{\text{PC}}$  data approach – did not improve the agreement results ( $r^2 = 0.45$ ,  $P < 0.0001$ ; bias =  $-0.14 \text{ L min}^{-1}$  and limits of agreement from 2.18 to  $-2.46 \text{ L min}^{-1}$ , i.e. 50% of the mean value). Throughout the entire surgical procedure, changes in

$\text{CO}_{\text{TD}}$  from baseline conditions (i.e. the first measurement after calibration) correlated better with changes in  $\text{CO}_{\text{PC}}$  ( $r^2 = 0.74$ ,  $P < 0.0001$ ) than with  $\text{CO}_{\text{echo}}$  ( $r^2 = 0.22$ ,  $P = 0.002$ ).

Administration of dobutamine resulted in a significant increase in  $\text{CO}_{\text{TD}}$ ,  $\text{CO}_{\text{PC}}$  and  $\text{CO}_{\text{echo}}$  (Table 1). The magnitude of changes in  $\text{CO}_{\text{TD}}$  was well reflected by  $\text{CO}_{\text{PC}}$  ( $\text{CO}_{\text{PC}} = 0.76 \times \text{CO}_{\text{TD}} + 0.58$ ;  $r^2 = 0.65$ ) and by  $\text{CO}_{\text{echo}}$ , although the latter tended to over-estimate these changes as shown by the slope exceeding unity ( $\text{CO}_{\text{echo}} = 1.58 \times \text{CO}_{\text{TD}} - 0.13$ ;  $r^2 = 0.53$ ) (Fig. 3).

## Discussion

This study demonstrates that the PulseCO™ system performs well as a non-invasive technique to measure CO during OPCAB surgery. Interestingly, this particular device can be connected to a peripheral blood pressure signal obtained from any standard arterial catheter and does not require specific disposables to be operational. The algorithm is different from other commercially available systems but until now, has not been extensively validated.

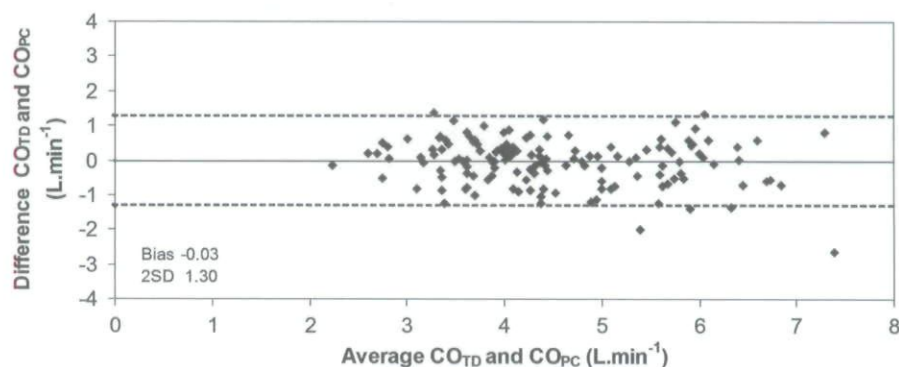


Figure 1.

Bland-Altman plot of cardiac output measurements by pulmonary artery thermodilution ( $\text{CO}_{\text{TD}}$ ) and pulse contour analysis ( $\text{CO}_{\text{PC}}$ ).

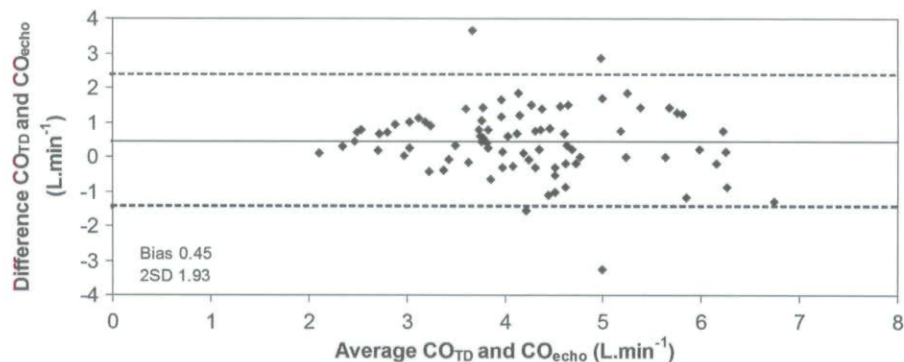


Figure 2.

Bland-Altman plot of cardiac output measurements by pulmonary artery thermodilution ( $\text{CO}_{\text{TD}}$ ) and transoesophageal echocardiography ( $\text{CO}_{\text{echo}}$ ).

The PulseCO<sup>TM</sup> PCA system requires *in vivo* calibration with an independent technique for which lithium dilution is being advocated by the manufacturer. Because we routinely use pulmonary artery catheters in OPCAB surgery, we had access to thermodilution data to calibrate the PulseCO system. Calibration was performed only once at the beginning of the procedure and the data of this study therefore reflect the independent performance of the system for a time period of at least 3 h.

In our clinical setting of OPCAB surgery, Doppler echocardiography was less accurate in quantifying CO. Previous studies have produced conflicting data on this subject, reporting excellent as well as poor agreement with thermodilution [9,10,15,16]. This discrepancy can partially be

explained by differences in the methodology, such as the choice of sampling location and the type of Doppler application used. From the different available modes, we preferred to interrogate trans-aortic flow using the continuous Doppler technique because this approach was shown to be most consistent in a recent comparative evaluation. Even when CO<sub>echo</sub> data were calibrated to match the first CO<sub>TD</sub> measurements, the accuracy did not improve. To our opinion, this suggests that CO<sub>echo</sub> errors result primarily from inaccuracies in the measurement of flow velocities, rather than aortic valve area calculation, because the latter should be corrected for by a single-point calibration. Our results are similar to data reported earlier in postcardiotomy patients in the ICU [10]. We found a 43% mean error, which matches exactly the data of Bettex and colleagues [10] and also exceeds the limit of clinical acceptability as proposed by Critchley and Critchley [14]. Apart from its suboptimal accuracy, however, the major limitation of transoesophageal echocardiography (TOE) in OPCAB surgery was the failure to obtain adequate transaortic Doppler signals when the heart was dislocated for exposure of the distal coronary territories. Nevertheless, the value of TOE in cardiac surgery clearly transcends its ability to quantify CO, and its role as a superior diagnostic and monitoring tool remains undisputed.

PCA devices, in contrast, are specifically designed to measure CO as a less invasive alternative to the pulmonary artery catheter. Accuracy is therefore an important prerequisite for clinical acceptance. Amongst the few commercially available PCA devices, the PiCCO system (Pulsion Medical Systems AG, Munich, Germany) has been validated

Table 1. Haemodynamic data (mean  $\pm$  SD) before and after a 15-min infusion of dobutamine at a rate of 2.5  $\mu\text{g kg}^{-1} \text{min}^{-1}$ .

	Before dobutamine	After dobutamine
APmean (mmHg)	66 $\pm$ 6	84 $\pm$ 12*
PAPmean (mmHg)	20 $\pm$ 4	23 $\pm$ 5
HR ( $\text{min}^{-1}$ )	59 $\pm$ 7	66 $\pm$ 5*
CVP (mmHg)	10 $\pm$ 3	9 $\pm$ 2
PaOP (mmHg)	14 $\pm$ 3	15 $\pm$ 4
CO <sub>TD</sub> ( $\text{L min}^{-1}$ )	4.1 $\pm$ 0.6	5.4 $\pm$ 0.5*
CO <sub>echo</sub> ( $\text{L min}^{-1}$ )	3.4 $\pm$ 0.7	5.6 $\pm$ 1.5*
CO <sub>PC</sub> ( $\text{L min}^{-1}$ )	4.1 $\pm$ 0.7	5.7 $\pm$ 0.4*

AP: arterial pressure; PAP: pulmonary artery pressure; HR: heart rate; CVP: central venous pressure; PaOP: pulmonary artery occlusion pressure; CO<sub>TD</sub>: cardiac output measured by thermodilution; CO<sub>echo</sub>: cardiac output measured by transoesophageal echocardiography; CO<sub>PC</sub>: cardiac output measured by pulse contour analysis.

\* $P < 0.05$  vs. value before dobutamine.

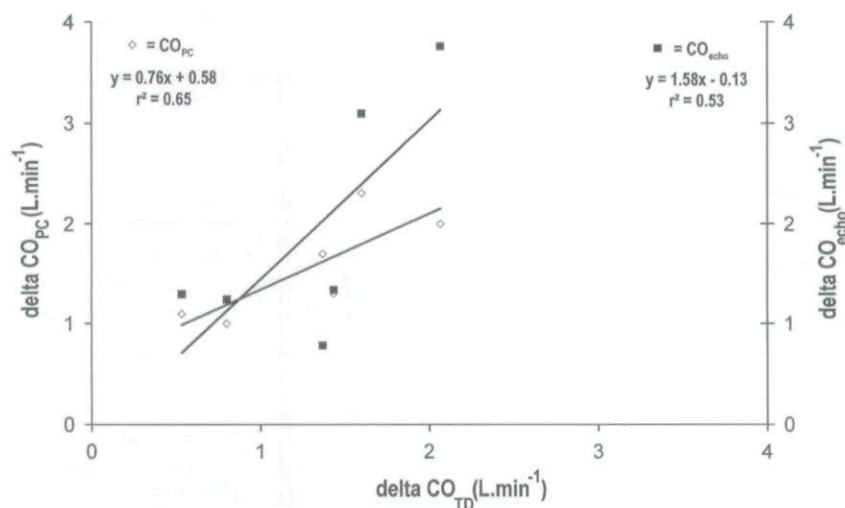


Figure 3.

Relationship between changes in thermodilution cardiac output (CO<sub>TD</sub>), pulse contour analysis cardiac output (CO<sub>PC</sub>) and transoesophageal echocardiography derived cardiac output (CO<sub>echo</sub>) before and after dobutamine administration.



most extensively. This device requires the use of a special catheter equipped with a thermistor to be inserted in, or advanced to a central arterial position such as the femoral, brachial or axillary site. PCA analysis from a peripheral arterial pressure signal is traditionally considered less accurate because curve damping and wave reflection can induce important errors. Nevertheless, data from the present study compare well to published data on accuracy with the PiCCO system and suggest that the PulseCO algorithm may be relatively insensitive to such artifacts [7,17,18]. We need to emphasize that our results were obtained in patients undergoing OPCAB surgery, a peculiar type of cardiac surgery for which extracorporeal circulation is not used. Cardiopulmonary bypass, in particular, when combined with moderate or deep hypothermia, is known to profoundly affect the peripheral arterial waveform [19]. Since it is currently not clear whether such conditions affect the accuracy of PulseCO, recalibration would certainly be required. We do believe that our results are relevant for the vast majority of patients undergoing major non-cardiac surgery for whom PAC catheters are often considered too invasive and PCA systems, calculating CO from a standard arterial pressure line, would be preferable.

The results of our study are clearly better than those previously published by Yamashita and colleagues [20] who used a similar approach in an almost identical clinical setting. These authors defined clinical acceptability of the difference between PCA and thermodilution to be within  $\pm 0.5 \text{ L min}^{-1}$ . This criterion might be too strict because the reference method itself is known to produce 10% inaccuracy [21]. For that reason, Critchley and Critchley [14] suggested that a percentage error of 30% would be a more reasonable limit for new methods when evaluated against thermodilution. The data of Yamashita and colleagues [20] contain one outlier with extremely high CO values, while data from the other patients appear consistent with ours. There was no obvious explanation for the major discrepancy in this patient. Identification and analysis of those clinical conditions associated with decreased accuracy require much larger study populations but are ultimately needed to fine-tune the current PCA algorithms.

The clinical value of a CO monitoring system also depends on its ability to monitor trends and to correctly quantify changes in CO. Only few studies have addressed this issue [18,22–24]. We administered low-dose dobutamine to a small number of patients after complete revascularization. PCA again appeared to be more accurate than TOE in quantifying the mild increases in CO.

We acknowledge that the sample size of our study was rather small and that not all possible testing conditions for PCA analysis were examined. For example, due to the small number of data points we could not prospectively test the assumption that different mechanisms of haemodynamic compromise would have different effects on accuracy. With regard to translation of our data to the general clinical field, we emphasize that we did not use the PulseCO PCA system in the mode it was designed for by the manufacturer. Instead of lithium dilution, we used thermodilution with a PA catheter to calibrate the PCA system because (1) clinical routine provided us with this opportunity and (2) we considered it to be superior from a methodological point of view. However, the simultaneous use of a PA catheter would obviously invalidate the clinical advantage of PCA being a non-invasive technique. Previous studies have extensively evaluated the accuracy of lithium dilution over a wide range of CO measurements [25]. Nevertheless, potential inaccuracies with this method when used to calibrate the PulseCO system, would affect absolute  $\text{CO}_{\text{PC}}$  values. However, they would have only minimal effects on its ability to track CO changes.

In conclusion, our findings suggest that in a clinically challenging condition such as off-pump coronary artery bypass grafting, the non-invasive PCA system of PulseCO performs well as a continuous CO monitor and shows acceptable agreement with thermodilution.

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